

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

NASSIF et al

Atty. Ref.: **1721-34**

Serial No. Unknown

Continuation of Serial No. **09/214,759**

Group:

Filed: **August 14, 2001**

Examiner:

For: **DNA AND PROTEINS OR PEPTIDES SPECIFIC OF THE
NEISSERIA MENINGITIDIS SPECIES BACTERIA,
METHOD FOR OBTAINING THEM AND THEIR
BIOLOGICAL APPLICATIONS**

* * * * *

August 14, 2001

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

PRELIMINARY AMENDMENT

Entry and consideration of the following amendments and remarks are requested.

IN THE SPECIFICATION

Amend the specification as follows.

Page 1, before the first line, insert the following:

--The present application is a continuation of application Serial No. 09/214,759, filed January 12, 1999, which is a 371 application of PCT/FR97/01295, filed July 11, 1997, and claims benefit of FR 96 08768, filed July 12, 1996.--

Page 6, delete the paragraph spanning lines 4-11, and insert the following therefor:

--The DNAs of the invention are characterized in that they are in all or part genes, with their reading frame, present in *Neisseria meningitidis*, but absent either from *Neisseria gonorrhoeae* and from *Neisseria lactamica*, with the exception of genes involved in the biosynthesis of the polysaccharide capsule, frpA, frpC, opc, por A, rotamase, the sequence IS1106 (Accession No. Z 11857 in the EMBL/GenBank/DBJ Nucleotide Sequence Data Libraries; see Knight et al., 1992, Molecular Microbiology 6(11): 1565-1573), IgA proteases, pilin, pilC, proteins which bind transferrin and opacity proteins.--

Page 20, delete the paragraph at line 8, and insert the following therefor:

--Reco24, 5' AGCACTCTCCAGCCTCTCACCGAG 3'; (= RBam 24, SEQ ID NO: 55)--.

Page 38, delete the paragraph bridging lines 1-6, and insert the following therefor:

--ORF-1: 1330 to 2970 (SEQ ID No. 37); ORF-2: 3083 to 9025 (SEQ ID No. 38); ORF-3: 9044 to 9472 (SEQ ID No. 39); ORF-4: 9620 to 12118 (SEQ ID No. 40); ORF-5: 12118 to 12603 (SEQ ID No. 42); ORF-6: 12794 to 13063 (SEQ ID No. 43); ORF-7: 13297 to 14235 (SEQ ID No. 44); and ORF-8: 14241 to 15173 (SEQ ID No. 45). --

Page 38, delete the paragraph spanning lines 7-9, and insert the following therefor:

--ORF-4 starts with the codon GTG and overlaps a slightly smaller ORF (SEQ ID No. 41) in the same reading frame (10127 - 12118, frame 2), which starts with the codon ATG.--

Insert the attached Sequence Listing for the Sequence Listing originally filed.

IN THE CLAIMS

Cancel claims 1-32, without prejudice.

Insert the following claims:

--33. (new) An isolated and purified DNA selected from the group consisting of at least one gene containing a reading frame present in *Neisseria meningitidis* (Nm), but absent either from *Neisseria gonorrhoeae* (Ng) or from *Neisseria lactamica* (Nl) such that said gene is Nm specific, and

a portion of said at least one gene, with the proviso that said portion is Nm specific,

provided that said DNA is not sequence IS1106 (accession number Z11857), *frpA*, *frpC*, *opc*, *porA*, *pilC*, a glutathione peroxidase-related gene, and a gene involved in the biosynthesis of any one of the polysaccharide capsule, rotamase, IgA proteases, pilin, a protein which binds transferrin or an opacity protein.

34. (new) A DNA according to claim 33, which is present in Nm, but absent from Ng.

35. (new) A DNA according to claim 34, comprising at least one isolated sequence selected from the group consisting of a sequence present in a region 1, said region 1 being the chromosome of Nm Z2491 between *tufA* and *pilT*, and at least one nucleotide sequence which hybridizes with said sequence, with the proviso that said sequence is present in Nm and absent from Ng.

36. (new) A DNA according to claim 34, comprising at least one isolated sequence selected from the group consisting of a sequence present in a region 2, said

region 2 being the chromosome of Nm Z2491 between *pilQ* and λ 740, and at least one nucleotide sequence which hybridizes with said sequence, with the proviso that said sequence is present in Nm and absent from Ng.

37. (new) A DNA according to claim 34, comprising at least one isolated sequence selected from the group consisting of a sequence present in a region 3, said region 3 being the chromosome of Nm Z2491 between *argF* and *opaB*, and at least one nucleotide sequence which hybridizes with said sequence, with the proviso that said sequence is present in Nm and absent from Ng.

38. (new) A DNA according to claim 35, comprising a sequence selected from the group consisting of:

- (i) SEQ ID NOs: 9, 13, 22, 30,
- (ii) a sequence of the chromosome of a Nm strain within ± 20 kb from a sequence selected from the group consisting of SEQ ID NOs: 9, 13, 22 and 30, and
- (iii) a sequence that hybridizes with at least one sequence selected from the group consisting of a sequence of (i) and (ii), with the proviso that said sequence that hybridizes is present in Nm and absent from Ng.

39. (new) A DNA according to claim 36, comprising a sequence selected from the group consisting of:

- (i) SEQ ID NOs: 1, 2, 4, 6, 7, 10, 15, 31, 34,
- (ii) a sequence of the chromosome of a Nm strain within ± 20 kb from a sequence selected from the group consisting of SEQ ID NOs: 1, 2, 4, 6, 7, 10, 15, 31, 34, and

(iii) a sequence that hybridizes with at least one sequence selected from the group consisting of a sequence of (i) and (ii), with the proviso that said sequence that hybridizes is present in Nm and absent from Ng.

40. (new) A DNA according to claim 36, comprising a sequence selected from the group consisting of:

(i) SEQ ID NO: 36, and a sequence encoding a sequence selected from the group consisting of SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 43, SEQ ID NO: 44, and SEQ ID NO: 45,

(ii) a sequence of the chromosome of a Nm strain within ± 20 kb from a sequence selected from the group consisting of SEQ ID NO: 36 and a DNA sequence encoding a sequence selected from the group consisting of SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 43, SEQ ID NO: 44, and SEQ ID NO: 45, and

(iii) a sequence that hybridizes with at least one sequence selected from the group consisting of a sequence as recited in the above (i) and (ii), with the proviso that said sequence that hybridizes is present in Nm and absent from Ng.

41. (new) A DNA according to claim 37, comprising a sequence selected from the group consisting of

(i) SEQ ID NO: 8, 21, 23, 25, 26, 28, 29, 32, 35,

(ii) a sequence of the chromosome of a Nm strain within ± 20 kb from a sequence selected from the group consisting of SEQ ID NO: 8, 21, 23, 25, 26, 28, 29, 32, and 35 on the chromosome of an Nm strain, and

(iii) a sequence that hybridizes with at least one sequence selected from the group consisting of a sequence of (i) and (ii) with the proviso that said sequence that hybridizes is present in Nm and absent from Ng.

42. (new) A DNA according to claim 34, comprising a sequence selected from the group consisting of:

(i) SEQ ID NOs: 3, 5, 11 12, 14, 16, 18, 19, 20, 24, 27, 33,

(ii) a sequence of the chromosome of a Nm strain within ± 20 kb from a sequence selected from the group consisting of SEQ ID NOs: 3, 5, 11 12, 14, 16, 18, 19, 20, 24, 27, and 33, and

(iii) a sequence that hybridizes with at least one sequence selected from the group consisting of a sequence of (i) and (ii), with the proviso that said sequence that hybridizes is present in Nm and absent from Ng.

43. (new) A DNA according to claim 33, which is an Ng sequence, but absent from NI.

44. (new) A DNA according to claim 43, comprising at least one sequence selected from the group consisting of a sequence present in a region 4, said region 4 being the chromosome of Nm Z2491 between *argJ* and *regF*, and at least one nucleotide sequence which hybridizes with said at least one sequence, with the proviso that said sequence is present in Nm and Ng but absent from NI.

45. (new) A DNA according to claim 43, comprising at least one sequence selected from the group consisting of a sequence present in a region 5, said region 5 being the chromosome of Nm Z2491 between the marker lambda 375 and *penA*, and at

least one nucleotide sequence which hybridizes with said at least one sequence, with the proviso that said sequence is present in Nm and Ng but absent from NI.

46. (new) A DNA according to claim 33, which codes for a protein exported beyond the cytoplasmic membrane in an Nm strain.

47. (new) A DNA according to claim 33, comprising at least a part of a sequence conserved within the Nm species.

48. (new) A transfer or expression vector comprising a DNA according to claim 33.

49. (new) A host cell transformed by at least one DNA according to claim 33.

50. (new) A cell wherein at least a part of a gene specific to Nm according to claim 33, has been deleted.

51. (new) An isolated and purified RNA, having a sequence comprising the transcription sequence of at least one DNA according to claim 33.

52. (new) An isolated and purified antisense nucleic acid sequence, which is the antisense of a DNA according to claim 33, and which optionally contains at least one chemical substituent.

53. (new) An isolated and purified polypeptide, having an amino acid sequence comprising a sequence coded by a DNA of claim 33, or deduced from a sequence of said DNA optionally containing modifications of said DNA which do not alter the biochemical properties observed in the natural polypeptide.

54. (new) A polypeptide according to claim 53, which is exported beyond the cytoplasmic membrane when expressed by a Nm cell.

55. (new) A method for diagnosis of a meningococcal infection, by detecting the presence of *Neisseria meningitis* in a biological sample, comprising the steps of:

contacting said sample with a reagent comprising at least one DNA of claim 33, optionally, in the form of a probe or a primer, under conditions which allow hybridization, and

detecting any hybridization.

56. (new) A kit comprising:

at least one DNA according to claim 33, and, optionally, markers or buffers or reagents to make markers or buffers, to enable at least one of a nucleotide hybridization reaction and detection of said reaction.

57. (new) A vaccine composition comprising a physiologically acceptable vehicle and an antimeningococcal prophylaxis effective amount of a polypeptide according to claim 53, said polypeptide being optionally conjugated.

58. (new) A vaccine composition comprising a physiologically acceptable vehicle, and an antimeningococcal prophylaxis effective amount of an agent selected from the group consisting of a DNA according to claim 33 and a cell containing a DNA according to claim 33.

59. (new) A composition comprising a DNA according to claim 33, in combination with a physiologically acceptable vehicle.

60. (new) An antisense nucleic acid sequence according to claim 52, wherein said chemical substituent is selected from the group consisting of a methyl group and a glycosyl group.

61. A vaccine composition according to claim 57, wherein said polypeptide is conjugated with a carrier molecule selected from the group consisting of poliovirus proteins, tetanus toxins, proteins produced by the hypervariable region of pilin.

62. A vaccine composition according to claim 57, further comprises a childhood vaccine.

63. (new) A DNA according to claim 36, comprising a sequence selected from the group consisting of SEQ ID NO: 38, a sequence of the chromosome of an Nm strain within ± 20 kb from SEQ ID NO: 38, and a sequence that hybridizes with SEQ ID NO: 38 with the proviso that said sequence that hybridizes is present in Nm and absent from Ng.

64. A DNA according to claim 43, comprising at least one sequence selected from the group consisting of SEQ ID. No. 67, 70, 74, 77, 79, 80, 84, 87, 88, 89, 92, 95, 96, 98, 99.--

REMARKS

Claims 1-32 have been canceled, without prejudice. Claims 33-64 have been added and are pending. Support for the amended claims may be found throughout the specification. No new matter has been added.

The present application has been referred to herein and in the attached as a "continuation" application, without prejudice.

The specification has been amended as previously in the parent application Serial No. 09/214,759. No new matter has been added.

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Serial No. Unknown
Continuation of Serial No. **09/214,759**

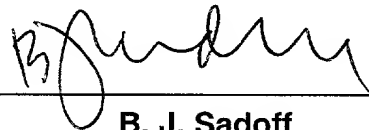
The specification has been amended to include the attached Sequence Listing. The attached paper copy of the Sequence Listing is the same as the paper and computer readable copies of the Sequence Listing filed in the parent application Serial No. 09/214,759. No new matter has been added. The Office is requested to use the computer readable form of the Sequence Listing from the parent application Serial No. 09/214,759, for the present application. A separate Request in this regard is attached.

An early and favorable Action on the merits is requested.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: _____



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MARKED UP SPECIFICATION AND CLAIMS

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